

201-14930

December 18, 2003

Via US Mail and e-mail

Administrator, Michael O. Leavitt
U.S. Environmental Protection Agency (EPA)
P.O. Box 1473
Merrifield, VA 22116

**Re: Rubber and Plastic Additives (RAPA) Panel,
HPV Chemical Challenge Program Submission
Sodium Dimethyldithiocarbamate (SDMC; CAS no. 128-04-1)
Test Plan & Robust Summaries**

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Dear Administrator Leavitt:

The RAPA Panel of the American Chemistry Council is pleased to submit the attached revised documents to EPA's High Production Volume (HPV) Chemical Challenge Program (Program) to fulfill our commitment for one of the 37 chemicals the RAPA Panel is voluntarily sponsoring in the Program. The RAPA Panel consists of the following member companies: Alco Chemicals; Bayer Polymers LLC; Ciba Specialty Chemicals Corporation; Crompton Corporation; Eliokem, Inc.; Flexsys America L.P.; The Goodyear Tire & Rubber Company; The Lubrizol Corporation; Noveon, Inc.; and, R.T. Vanderbilt Company, Inc.

This submission consists of a Test Plan and Robust Summaries for Sodium Dimethyldithiocarbamate (SDMC; CAS no. 128-04-1).

In addition to the *Test Plan*, please also find attached robust summaries contained in IUCLID-formatted documents for SDMC.

This submission is also being sent electronically to the following e-mail addresses:

Oppt.ncic@epa.gov
Chem.rtk@epa.gov

If you require additional information, please contact the RAPA Panel's technical contact, Dr. Anne P. LeHuray at (703) 741-5630 or anne_lehuray@americanchemistry.com.

Sincerely yours,

Attachments

201-14930A

Test Plan Sodium Dimethyldithiocarbamate

CAS Registry Number 128-04-1

Rubber and Plastic Additives Panel
American Chemistry Council
December 2003

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List of Member Companies in the Rubber and Plastic Additives Panel

The Rubber and Plastic Additives Panel of the American Chemistry Council includes the following member companies: Alco Chemicals, Bayer Polymers LLC, Ciba Specialty Chemicals Corporation, Crompton Corporation, Eliokem, Inc., Flexsys America L.P., The Goodyear Tire & Rubber Company, The Lubrizol Corporation, Noveon, Inc., and R.T. Vanderbilt Company, Inc.

Summary

The member companies of the American Chemistry Council's Rubber and Plastic Additives Panel (RAPA) hereby submit for review and public comment their test plan for sodium dimethyldithiocarbamate (SDMC; CAS no. 128-04-1) under the High Production Volume (HPV) Chemical Challenge Program.

SDMC is used as a water treatment chemical; it precipitates heavy metal ions from water. It is used in the rubber industry to stop quickly the polymerization of synthetic (SBR) latexes. It is also a registered biocide for cutting oils and aqueous systems such as leather tanning and paper manufacturing.

Existing data for this compound indicate that it is of low concern for mammalian toxicity but toxic to most aquatic organisms. SDMC is of moderate concern for skin irritation and allergic skin reaction.

The RAPA Panel concludes that there are sufficient data on SDMC to meet the requirements of the HPV Chemical Challenge Program and no additional testing is recommended.

Aquatic Toxicology. SDMC is toxic to aquatic organisms. There are several studies on SDMC, and while results vary they indicate the potential hazard of this product. The 48-hr EC_{50} for *Daphnia* is 1.5 ppm; the 96-hr LC_{50} for rainbow trout was 0.85 mg/l in one study and 6.7 mg/l in a second study. The 96-hr LC_{50} for bluegill sunfish was 3.3 mg/l in one study and 38.5 mg/l in a second. The 96-hr LC_{50} for Sheepshead minnows was 60.1 mg/l. The 96-hr

EC50 for algae (*Chlorella pyrenoidosa*) is 0.8 mg/l.

SDMC is biodegradable; the main breakdown products are tetramethyl thiuram mono- and disulfides which, in turn, break down in water.

Acceptable data are available on toxicity to algae, toxicity to aquatic invertebrates, toxicity to fish and biodegradability. The data warrant handling the product as an environmentally hazardous substance. Adequate data exist in SIDS endpoints, so no additional ecotoxicity testing is proposed.

Acute Toxicity: The acute oral and dermal LD₅₀s for SDMC are >2000 mg/kg; the acute inhalation LC₅₀ is >2.05 mg/l for four hours. Since acceptable data are available on three routes of exposure, no additional acute toxicity testing is proposed.

Mutagenicity: Several genetic toxicity studies have been conducted on SDMC. In an Ames assay, SDMC was mutagenic in three strains of *Salmonella* (TA 100, TA 1535 and TA 1537). However, no genotoxic effects were observed in a rat liver unscheduled DNA synthesis assay. Based on this data the RAPA Panel concludes that SDMC is weakly mutagenic to bacteria but not mutagenic to mammalian cells *in vitro* and that no additional mutagenicity testing is warranted.

Repeated Dose Toxicity: A 90-day dermal toxicity study in rabbits was performed on SDMC. Dermal irritation was observed at dosing site in mid- and high-dose group animals. There was no histologic evidence of systemic toxicity in any group of animals. White blood cell and platelet count were reduced at the high dose level.

An 18-month chronic toxicity and carcinogenicity study in mice was conducted on a close structural analogue, sodium diethyldithiocarbamate. The results of this study were classified "equivocal." Oral administration of the test compound at the maximum tolerated dose resulted in an elevation of tumor incidence in an uncertain range. The positive control chemicals produced the expected incidence and types of tumors in the test animals. The study authors suggest that either additional statistical evaluation and/or experimentation would be required before a more exact interpretation can be made.

A two-year chronic toxicity and carcinogenicity study in rats and mice was conducted on a close structural analogue, sodium diethyldithiocarbamate. No tumors occurred in either rats or mice of either sex at incidences that were significantly higher in dosed animals than in controls. The study concluded that sodium diethyldithiocarbamate is not carcinogenic to rats or mice of either sex.

These data are acceptable to characterize the subchronic and chronic toxicity of SDMC for the HPV Chemical Challenge Program. No additional subchronic or chronic toxicity testing is proposed for SDMC.

Reproductive and Developmental Toxicity: Developmental toxicity studies on SDMC have been conducted with rabbits and rats. In both cases the No Observed Effect Level (NOEL) for

maternal toxicity was lower than the NOEL for developmental toxicity. A multi-generation rat reproductive toxicity study on a close structural analogue, sodium monomethyldithiocarbamate (Metam sodium) has also been conducted. Metam sodium (43.148% w/w) was given in drinking water at 0, 0.01, 0.03 or 0.10 mg metam sodium/ml to Alpk:APfSD rats (30/sex/dose) for two generations. The parental systemic NOEL was 0.01 mg/ml; decreased food consumption, water consumption and body weight in both sexes of both parental generations were observed at 0.1 mg/ml. Females in the F1 parental generation also showed a decrease in water consumption at 0.03 mg/ml. Histopathology in the nasal cavity was reported (Bowman's duct hypertrophy with loss of alveolar cells, disorganization/degeneration/atrophy of olfactory epithelium, hyperplasia of olfactory epithelium and dilatation of ducts of Bowman's glands) at 0.1 mg/ml. The parental reproductive NOEL is greater than 0.1 mg/ml; there were no significant reproductive effects at any dose. The pup NOEL was 0.03 mg/ml; pups showed a tendency at 0.1 mg/ml to have decreased body weight from day 22 (males) in the F1a generation and from day 5 (males) in the F2a generation.

These studies provide evidence that SDMC is not a selective or specific reproductive or developmental toxin. No additional reproductive or developmental testing is proposed for these materials.

Conclusion: The physical, chemical and toxicological properties of sodium dimethyldithiocarbamate have been considerably studied. A detailed hazard analysis can be made with the data available; additional studies would not significantly change what is already known about this product. Therefore, the RAPA Panel concludes that there are sufficient data on this compound to meet the requirements of the HPV Chemical Challenge Program and recommend no additional testing.

Background Information: Manufacturing and Commercial Applications

Manufacturing

SDMC has been manufactured world wide for over 60 years. It is manufactured by batch rather than continuous process. SDMC is manufactured by combining dimethylamine with carbon disulfide in a solution of sodium hydroxide, forming the water-soluble dithiocarbamate salt.

Commercial Applications

SDMC is used to precipitate heavy metal ions from water. As a free-radical inhibitor, it is used in the rubber industry to stop quickly the polymerization of synthetic (styrene-butadiene rubber, or SBR) latexes. It is also used as a biocide for cutting oils and aqueous systems such as leather tanning and paper manufacturing.

Worker/Consumer Exposure

The majority of SDMC is used for water treatment, where only sophisticated industrial users handle this material. Most large industrial users have mechanized materials handling systems, so exposure is generally minimal. The greatest potential for skin and inhalation exposure is at

the packing station at the manufacturing site and, to a somewhat lesser degree during weighing activities at the customer site.

SDMC is regulated for use in food-contact applications by the Food and Drug Administration as follows.

21 CFR 177.2600, Rubber articles intended for repeated use: As accelerator, not to exceed 1.5% by weight of rubber product.

21 CFR 176.300, Slimicides.

21 CFR 175.105, Components of Adhesives.

21 CFR 173.320, Chemicals for controlling microorganisms in cane-sugar and beet-sugar mills.

SODIUM DIMETHYLDITHIOCARBAMATE (SDMC) Test Plan

CAS No. 128-04-1

Rubber and Plastic Additives Panel
December 2003

Physical-Chemical					
Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient	Water Solubility	
A	A	Calc	Calc	A	
Environmental Fate					
Photodegradation	Stability in Water	Transport/ Distribution	Biodegradation		
Calc	A	Calc	A		
Ecotoxicity					
Acute Toxicity to Fish		Acute Toxicity to Aquatic Plants (e.g., Algae)		Acute Toxicity to Aquatic Invertebrates (e.g., <i>Daphnia</i>)	
A		A		A	
Mammalian Toxicity					
Acute Toxicity	Bacterial Genetic Toxicity <i>In Vitro</i>	Mammalian Genetic Toxicity <i>In Vivo</i>	Repeat Dose Toxicity	Reproductive Toxicity	Developmental Toxicity
A	A	NR	A	SAR	A

Legend	
Symbol	Description
Test	Endpoint requirements to be fulfilled with testing
Calc	Endpoint requirement fulfilled based on calculated data
A	Endpoint requirement fulfilled with adequate existing data
NR	Not required per the OECD SIDS guidance
NA	Not applicable due to physical/chemical properties
SAR	Structure-Activity Relationship

CAS# 128-04-1
Carbamodithioic acid, dimethyl-, sodium salt

Molecular Formula: $C_3H_7NS_2 \cdot Na$
Molecular Weight: 144.2

201-14930B

1.1 **GENERAL SUBSTANCE INFORMATION**

A. **Type of Substance:** Organic
B. **Physical State:** Yellow liquid
C. **Purity:** Typically 40% w/w as aqueous solution

1.2 **SYNONYMS** Methyl Namate®
SDMC
SDDC
Aquatreat® SDM
Perkacit® SDMC

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PHYSICAL-CHEMICAL DATA

***2.1 MELTING POINT**

Value: 110° C (isolated solid)
Decomposition: No
Sublimation: No
Method: Differential Scanning Calorimetry
GLP: Yes
Remarks:
Reference: R. T. Vanderbilt study; Baron Consulting, 1990
Reliability: (1) Valid without restriction

***2.2 BOILING POINT**

Value: 102° C (32% aqueous solution)
Pressure: 1 Atmosphere
Decomposition: No data
Method: No data
GLP: Yes
Remarks:
Reference: R. T. Vanderbilt study; Baron Consulting, 1990
Reliability: (1) Valid without restriction

†2.3 DENSITY (relative density)

Type: Density
Value: 1.14 (32% aqueous solution)
1.43 (isolated solid)
Temperature: 20° C
Method: No data
GLP: Yes
Remarks:
Reference: R. T. Vanderbilt study; Baron Consulting, 1990
Reliability: (1) Valid without restriction

***2.4 VAPOUR PRESSURE**

Value: 3.7 x 10⁻⁸ mm Hg
 Temperature: 25° C
 Method: calculated
 Other: Modified Grain method
 GLP: No
 Remarks: Estimation method based on molecular structure and measured melting point value.
 Reference: EPIWIN/MPBPWIN v1.40
 Reliability: (2) Valid with restrictions – modelling data

***2.5 PARTITION COEFFICIENT log₁₀P_{ow}**

Log Pow: -2.41
 Temperature: None
 Method: calculated
 Other: SRC LogKow (KowWin) Program 1995
 GLP: No
 Remarks: Estimation method based on molecular structure and measured melting point value.
 Reference: EPIWIN/KOWWIN v1.66
 Reliability: (2) Valid with restrictions – modelling data

***2.6 WATER SOLUBILITY**

A. Solubility

Value: miscible
 Temperature: 20° C
 Method: No data
 GLP: Yes
 Remarks:
 Reference: R. T. Vanderbilt study; Baron Consulting, 1990
 Reliability: (1) Valid without restriction

B. pH Value, pKa Value

pH Value: 10.1 (1% aqueous solution)
 12.6 (32% aqueous solution)
 pKa value: Not applicable; product decomposes below pH 8.

2.11 OXIDIZING PROPERTIES

†2.12 OXIDATION: REDUCTION POTENTIAL

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

B. Other data – Henry's Law Constant

Results: 6.972 x 10⁻¹⁵ atm-m³/mole
 Remarks: Calculated value from moist soil surfaces. Estimation method based on molecular structure and measured melting point value.
 Reference: Environ Toxicol Chem 10: 1283-93 (1991)
 EPIWIN/HENRYWIN v3.10
 Reliability: (2) Valid with restrictions – modelling data

3. ENVIRONMENTAL FATE AND PATHWAYS

*3.1.1 PHOTODEGRADATION

Type: Air
Light source: Sunlight
Temperature: 25°C
Direct photolysis:
Half life: 0.925 hours
Indirect Photolysis:
Rate constant (radical): $68.5296 \times 10^{-12} \text{ cm}^3/\text{molecule-sec}$
Method: calculated
Atmospheric Oxidation Program/SAR Methods, 1995
GLP: No
Test substance: Other: SAR
Remarks: Half-life estimated to be 0.156 days (12-hr day, $1.5 \times 10^6 \text{ OH/cm}^3$) or 1.873 hours. Estimation method based on molecular structure and measured melting point value.
Reference: Meylan, WH and Howard, PH, Chemosphere 26: 1193-99, 1999
EPIWIN/AOPWIN v1.90
Reliability: (2) Valid with restrictions – modelling data

*3.1.2 STABILITY IN WATER

Type: Hydrolysis as a function of pH
Media: Water buffered to pH 5, 7 and 9
Method: OPPTS 835.2110
Results: estimated half life:
pH 5.0: 0.30 hr (18 min)
pH 7.0: 25.9 hr (1,555 min)
pH 9.0: 433.3 hr (25,997 min)
Remarks: Additional study information is confidential and compensable under FIFRA.
Reference: Alco Chemical Division, National Starch and Chemical Company; Hazleton Laboratories America, 1987
Reliability: (1) Valid without restrictions

Type: Volatility
Media: Water
Method: Estimation Method, 1990
Results: Volatilization half-life from model river: 1.15×10^7 years
Volatilization half-life from model lake: 1.25×10^8 years
Remarks: Model river = 1 m deep flowing at 1 m/sec and wind velocity of 5 m/sec. Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec.
Reference: Alco Chemical Division, National Starch and Chemical Company; Hazleton Laboratories America, 1987
Reliability: (2) Valid with restrictions – modelling data

***3.2 MONITORING DATA (ENVIRONMENTAL)**

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

***3.3.1 TRANSPORT**

Type: Adsorption/desorption
Media: Soil/Sediment
Method: OPPTS 835.1230
Results:

Adsorption coefficients (Kd):

sandy loam: 5.99
silt loam: 12.6
silty clay loam: 6.47
sand: 1.45

Desorption:

sandy loam: 0 – 19.7%
silt loam: 8.6 – 17.8%
silty clay loam: 1.1 – 21.9%

Remarks: Additional study information is confidential and compensable under FIFRA
Reference: Alco Chemical Division, National Starch and Chemical Company; Hazleton Laboratories America, 1986
Reliability: (1) Valid without restrictions

Type: Volatility
Media: Water
Method: Estimation Method, 1990
Results: Volatilization half-life from model river: 1.15×10^7 years
Volatilization half-life from model lake: 1.25×10^8 years
Remarks: Model river = 1 m deep flowing at 1 m/sec and wind velocity of 5 m/sec. Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec. Estimation method based on molecular structure and measured melting point value.
Reference: Handbook of Chemical Property Estimation Methods, 1990
Reliability: (2) Valid with restrictions – modelling data

***3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)**

Media: Air-biota-sediment-soil-water
Method: Fugacity level III
EPIWIN v3.10

Results:	Mass Amount (%)	Half-life (hrs)	Emissions (kg/hr)
Air	1.02×10^{-6}	3.75	1000
Water	45.3	360	1000
Soil	54.6	360	1000
Sediment	0.0755	1440	0

Remarks:	Persistence time estimated at 421 hours. Estimation method based on molecular structure and measured melting point value.
Reference:	EPISUITE/EPIWIN v3.10
Reliability:	(2) Valid with restrictions – modelling data

***3.5 BIODEGRADATION**

Species:	None
Exposure Period:	96 days
Temperature:	25° C
Concentration:	9.2 ppm
Method:	OPPTS 835.4400
Type of test:	Anaerobic degradation
GLP:	Yes
Test substance:	¹⁴ C-labelled SDMC
Remarks:	Tetramethyl thiuram disulfide, tetramethyl thiuram monosulfide were the major decomposition products. Additional study information is confidential and compensable under FIFRA.
Reference:	Alco Chemical Division, National Starch and Chemical Company; Hazleton Laboratories America, 1987
Reliability:	(1) Valid without restrictions

3.6 BOD5, COD OR RATIO BOD5/COD

3.7 BIOACCUMULATION

Species:	None
Exposure Period:	None
Temperature:	None
Concentration:	None
BCF:	0.5 (estimated)
Elimination:	
Method:	Calculated
Type of test:	
GLP:	No
Test substance:	
Remarks:	
Reference:	EPISUITE/EPIWIN BCF Program v2.14
Reliability:	(2) Valid with restrictions – modelling data

4. ECOTOXICITY

***4.1 ACUTE TOXICITY TO FISH**

Type of test:	Flow-through
Species:	<i>Cyprinodon variegatus</i> (Sheepshead minnow)
Exposure period:	96 hours
Results:	LC ₅₀ (24h) = 107 mg/l LC ₅₀ (48h) = 63.0 mg/l LC ₅₀ (72h) = 60.1 mg/l

LC_{50} (96h) = 60.1 mg/l
 $NOEC$ = 23.9 mg/l
 Analytical monitoring: Yes
 Method: FIFRA 72-3
 GLP: Yes
 Test substance: As prescribed by 1.1-1.4, purity 48.27% w/v
 Remarks: Additional study information is confidential and compensable under FIFRA.
 Reference: Alco Chemical Division, National Starch and Chemical Company; Toxikon Environmental Sciences
 Reliability: (1) Valid without restriction

Type of test: Flow-through
 Species: *Oncorhynchus mykiss* (Rainbow trout)
 Exposure period: 96 hours
 Results: LC_{50} (24h) = 32.2 mg/l
 LC_{50} (48h) = 7.12 mg/l
 LC_{50} (72h) = 6.69 mg/l
 LC_{50} (96h) = 6.69 mg/l
 $NOEC$ < 3.66 mg/l

Analytical monitoring: Yes
 Method: FIFRA 72-1
 GLP: Yes
 Test substance: As prescribed by 1.1-1.4, purity 48.27% w/v
 Remarks: Additional study information is confidential and compensable under FIFRA.
 Reference: Alco Chemical Division, National Starch and Chemical Company; Toxikon Environmental Sciences (03/10/1992)
 Reliability: (1) Valid without restriction

Type of test: Static
 Species: *Salmo gairdneri* (*Oncorhynchus mykiss*, rainbow trout)
 Exposure period: 96 hours
 Results: LC_{50} (24h) = 7.6 mg/l
 LC_{50} (48h) = 1.5 mg/l
 LC_{50} (96h) = 0.85 mg/l
 $NOEC$ 0.3 mg/l

Analytical monitoring: Not reported
 Method: EPA OPPTS 40 CFR 850.1075
 GLP: Yes
 Test substance: Aquatreat SDM, SDMC 40%
 Remarks: Additional study information is confidential and compensable under FIFRA.
 Reference: Alco Chemical Division, National Starch and Chemical Company; Analytical Bio-Chemistry Laboratories, Inc. (1985)
 Reliability: (1) Valid without restriction

Type of test: Static
 Species: *Lepomis macrochirus* (Bluegill)
 Exposure period: 96 hours
 Results: LC_{50} (24h) = 23 mg/l
 LC_{50} (48h) = 4.0 mg/l
 LC_{50} (96h) = 3.3 mg/l

NOEC < 0.6 mg/l

Analytical monitoring: Yes

Method: EPA OPPTS 40 CFR 850.1075

GLP: Yes

Test substance: Aquatreat SDM, SDMC 40%

Remarks: Additional study information is confidential and compensable under FIFRA.

Reference: Alco Chemical Division, National Starch and Chemical Company; Analytical Bio-Chemistry Laboratories, Inc. (1985)

Reliability: (1) Valid without restriction

Type of test: Flow-through

Species: *Lepomis macrochirus* (Bluegill)

Exposure period: 96 hours

Results: LC₅₀ (96h) = 38.5 mg/l
NOEC = 6.40 mg/l

Analytical monitoring: Yes

Method: FIFRA 72-1

GLP: Yes

Test substance: Aquatreat SDM, purity 47.75% w/v (40.47% SDMC w/w)

Remarks: Additional study information is confidential and compensable under FIFRA.

Reference: Alco Chemical Division, National Starch and Chemical Company; Toxikon Environmental Sciences (03/10/1992)

Reliability: (1) Valid without restriction

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

***A. Daphnia**

Type of test: Flow-through

Species: *Daphnia magna*

Exposure period: 48 hours

Results: EC₅₀ (48h) = 0.0715 mg/l
NOEC = 0.0104 mg/l

Analytical monitoring: Yes

Method: FIFRA 77-2

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity 40.47% w/w

Remarks: Additional study information is confidential and compensable under FIFRA.

Reference: Alco Chemical Division, National Starch and Chemical Company; Toxikon Environmental Sciences 10/02/1992

Reliability: (1) Valid without restriction

Type of test: Static

Species: *Daphnia magna*

Exposure period: 48 hours

Results: EC₅₀ (48h) = 0.0715 mg/l
NOEC = 0.0104 mg/l

Analytical monitoring: Yes

Method: FIFRA 77-2

GLP: Yes

Test substance:	As prescribed by 1.1-1.4, purity 40.47% w/w
Remarks:	Additional study information is confidential and compensable under FIFRA.
Reference:	Alco Chemical Division, National Starch and Chemical Company; Toxikon Environmental Sciences 10/02/1992
Reliability:	(1) Valid without restriction
Type of test:	Static
Species:	<i>Daphnia magna</i>
Exposure period:	48 hours
Results:	LC ₅₀ (48h) = 1.5 mg/l NOEC < 0.18 mg/l
Analytical monitoring:	Yes
Method:	OPPTS 850.1010
GLP:	Yes
Test substance:	As prescribed by 1.1, purity 40% w/w
Remarks:	Additional study information is confidential and compensable under FIFRA.
Reference:	Alco Chemical Division, National Starch and Chemical Company; Analytical Bio-chemistry Laboratories, Inc., 1985
Reliability:	(1) Valid without restriction
Type of test:	Static
Species:	<i>Mysidopsis bahia</i>
Exposure period:	96 hours
Results:	LC ₅₀ (96h) = 2.7 µg/l NOEC = 0.64 µg/l
Analytical monitoring:	Yes
Method:	OPPTS 850.1055
GLP:	Yes
Test substance:	As prescribed by 1.1, purity 40% w/w
Remarks:	Additional study information is confidential and compensable under FIFRA.
Reference:	Alco Chemical Division, National Starch and Chemical Company; Springborn Bionomics, Inc., 1987
Reliability:	(1) Valid without restriction

***4.3 TOXICITY TO AQUATIC PLANTS, e.g. algae**

Type of test:	Static
Species:	<i>Chorella pyrenoidosa</i>
Exposure period:	96 hours
Results:	EC ₅₀ (96h) = 0.8 mg/l
Analytical monitoring:	No data
Method:	OECD 201
GLP:	No data
Test substance:	As prescribed by 1.1, purity 40% w/w
Remarks:	None
Reference:	Van Leeuwen, C.J., Ecotoxicological Aspects of Dithiocarbamates. Rijkswaterstaat, Publication No. 44/1986
Reliability:	(1) Valid without restriction

***4.4 TOXICITY TO MICROORGANISMS, e.g. bacteria**

***4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS**

Type of test: Flow-through
Species: *Daphnia magna*
Exposure period: 48 hours
Results: EC₅₀ (48h) = 0.0715 mg/l
NOEC = 0.0104 mg/l
Analytical monitoring: Yes
Method: FIFRA 77-2
GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity 40.47% w/w
Remarks: Additional study information is confidential and compensable under FIFRA.
Reference: Alco Chemical Division, National Starch and Chemical Company; Toxikon Environmental Sciences 10/02/1992
Reliability: (1) Valid without restriction

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test: Flow-through
Species: *Daphnia magna*
Exposure period: 21 days
Results: EC₅₀ (48h) = 0.0715 mg/l
NOEC = 0.0104 mg/l
Analytical monitoring: Yes
Method: Other; laboratory-developed method based on EPA, OECD and ASTM guidelines
GLP: Yes
Test substance: As prescribed by 1.1, purity 40% w/w
Remarks: Tested at 0, 0.009, 0.021, 0.048, 0.080 and 0.19 mg/l. Survival and length were significantly reduced at 0.021 mg/l and higher. Additional study information is confidential and compensable under FIFRA.
Reference: Alco Chemical Division, National Starch and Chemical Company; Analytical Bio-Chemistry Laboratories, Inc. (1985)
Reliability: (1) Valid without restriction

5. TOXICITY

***5.1 ACUTE TOXICITY**

5.1.1 ACUTE ORAL TOXICITY

Type: LD₅₀
Species/strain: Rats, Sprague-Dawley
Value: 3929 mg/kg bw
Discriminating dose: 1850 mg/kg bw

Sex:	Male/female
# of Animals:	Five per sex per group
Vehicle:	None
Doses:	1850, 2500, 3500 and 5000 mg/kg bw
Method:	FIFRA 81-1
GLP:	Yes
Test substance:	Vancide® 51 (27.6% SDMC, 2.4% SMBT aqueous solution, pH 11.6).
Remarks:	Additional study information is confidential and compensable under FIFRA.
Reference:	R. T. Vanderbilt study; Springborn Laboratories, 1973
Reliability:	(1) Valid without restrictions.

5.1.2 ACUTE INHALATION TOXICITY

Type:	Limit test
Species/strain:	Rats, Sprague-Dawley
Value:	> 2.05 mg/l
Sex:	Male/female
# of Animals:	Five per sex per group
Vehicle:	None
Doses:	2.05 mg/l for four hours
Method:	FIFRA 81-3
GLP:	Yes
Test substance:	Vancide® 51 (27.6% SDMC, 2.4% SMBT aqueous solution, pH 11.6).
Remarks:	Additional study information is confidential and compensable under FIFRA.
Reference:	R. T. Vanderbilt study; Springborn Laboratories, 1973
Reliability:	(1) Valid without restrictions.

5.1.3 ACUTE DERMAL TOXICITY

Type:	Limit test
Species/strain:	Rabbits, New Zealand Albino
Sex:	Male/female
# of Animals:	Five per sex
Vehicle:	None
Doses:	2000 mg/kg bw
Exposure Time:	24 Hours
Value:	>2000 mg/kg bw
Method:	FIFRA 81-2
GLP:	Yes
Test substance:	Vancide® 51 (27.6% SDMC, 2.4% SMBT aqueous solution, pH 11.6)
Remarks:	No animals died during the study. The dermal LD50 is greater than 2000 mg/kg.
Reference:	R. T. Vanderbilt Study; Springborn Laboratories 1995
Reliability:	(1) Valid without restrictions

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

Species/strain: Rabbits, New Zealand Albino
Sex: Male/female
of Animals: Six
Exposure time: Four hours
Results: Slightly irritating
Classification: Not irritating
Method: FIFRA 81-5
GLP: Yes
Test substance: Vancide® 51 (27.6% SDMC, 2.4% SMBT aqueous solution, pH 11.6)
Remarks: 0.5 ml of the test substance was applied to the shaved skin of six albino rabbits for four hours. The mean Primary Irritation Index was 1.67. Additional study information is confidential and compensable under FIFRA.
Reference: R. T. Vanderbilt Study, Springborn Laboratories 1995
Reliability: (1) Valid without restrictions

Species/strain: Rabbits, New Zealand Albino
Sex: Male/female
of Animals: Six
Exposure time: Four hours
Results: Slightly irritating
Classification: Not irritating
Method: FIFRA 81-5
GLP: Yes
Test substance: Aquatreat SDM, 39.7% SDMC aqueous solution, pH 13.0)
Remarks: 0.5 ml of the test substance was applied to the shaved skin of six albino rabbits for four hours. The Primary Irritation Index was 1.0. Additional study information is confidential and compensable under FIFRA.
Reference: Alco Chemical Division, National Starch and Chemical Company; Stillmeadow Incorporated, 1995
Reliability: (1) Valid without restrictions

Species/strain: Rabbits, New Zealand Albino
Sex: Male/female
of Animals: Six
Exposure time: Four hours
Results: Slightly irritating
Classification: Not irritating
Method: FIFRA 81-5
GLP: Yes
Test substance: Aquatreat SDM, 39.7% SDMC aqueous solution, pH 13.0)
Remarks: 0.5 ml of the test substance was applied to the shaved skin of six albino rabbits for four hours. The Primary Irritation Index was 1.2. Additional study information is confidential and compensable under FIFRA.
Reference: Alco Chemical Division, National Starch and Chemical Company; Hazleton Laboratories America, Incorporated, 1986
Reliability: (1) Valid without restrictions

5.2.2 EYE IRRITATION/CORROSION

Species/Strain: Rabbits, New Zealand Albino
Sex: Male/female
of Animals: Nine
Results: Slightly irritating
Classification: Not irritating
Method: FIFRA 81-4
GLP: Yes
Test substance: Vancide® 51 (27.6% SDMC, 2.4% SMBT aqueous solution, pH 11.6)
Remarks: 0.1 ml of the test substance was applied to the eyes of nine albino rabbits; after 30 seconds, the eyes of three animals were washed with physiological saline. Irritation and corneal involvement was noted for up to 7 days; washing reduced the duration of the irritation. Additional study information is confidential and compensable under FIFRA.
Reference: R. T. Vanderbilt Study, Springborn Laboratories 1995
Reliability: (1) Valid without restrictions

Species/Strain: Rabbits, New Zealand Albino
Sex: Male/female
of Animals: Nine
Results: Mild to moderate irritation
Classification: Irritant
Method: FIFRA 81-4
GLP: Yes
Test substance: Aquatreat NM
Remarks: 0.1 ml of the test substance was applied to the eyes of nine albino rabbits; after 30 seconds, the eyes of three animals were washed with physiological saline. Conjunctival irritation and corneal involvement was noted in two of six unwashed eyes for up to 21 days; washing did not appear to reduce the degree or duration of the irritation. Additional study information is confidential and compensable under FIFRA.
Reference: Alco Chemical Division, National Starch and Chemical Company; Biosearch Incorporated, 1983
Reliability: (1) Valid without restrictions

*5.4 REPEATED DOSE TOXICITY

Species/strain: Rats, Sprague-Dawley
Sex: Male/Female
Route of Administration: Aqueous gavage
Exposure period: 13 Weeks
Frequency of treatment: Consecutive days
Post exposure observation period: No data
Dose: 0, 0.5, 5 or 250 mg/kg bw
Control group: Yes , concurrent vehicle
NOEL: Not Determined
LOEL: 5 mg/kg bw

Results: Administration of the test substance resulted in no functional or structural neurotoxicity. Additional study information is confidential and compensable under FIFRA.

Method: FIFRA 82-7

GLP: Yes

Test substance: Aquatreat SDM

Reference: SDDC/KDDC Task Force study; WIL Research Laboratories, Inc, 1/18/1995

Reliability: (1) Valid without restrictions

Species/strain: Rabbit, New Zealand White

Sex: Male/Female

Route of Administration: Dermal

Exposure period: 90 days

Frequency of treatment: Once per day, five days per week, thirteen weeks

Post exposure observation period: none

Dose: 0, 50, 150, 300 mg/kg/day as supplied (0, 20, 60, 120 mg/kg/day as SDMC)

Control group: Yes, concurrent untreated

NOEL: 50 mg/kg/day as supplied (20 mg/kg/day as SDMC)

LOEL: 150 mg/kg/day as supplied (60 mg/kg/day as SDMC)

Results: Dermal irritation was observed at dosing site in mid- and high-dose group animals. There was no histologic evidence of systemic toxicity in any group of animals. White blood cell and platelet count were reduced at the high dose level. Additional study information is confidential and compensable under FIFRA.

Method: FIFRA 82-3

GLP: Yes

Test substance: Aquatreat SDM sodium dimethyldithiocarbamate 40% aqueous solution

Reference: Alco Chemical Division, National Starch and Chemical Company; Exxon Biomedical Sciences Incorporated, 1986

Reliability: (1) Valid without restrictions

Species/strain: Rabbit, New Zealand White

Sex: Male/Female

Route of Administration: Dermal

Exposure period: 90 days

Frequency of treatment: Once per day, five days per week, thirteen weeks

Post exposure observation period: none

Dose: 0, 50, 150, 300 mg/kg/day as supplied (0, 20, 60, 120 mg/kg/day as SDMC)

Control group: Yes, concurrent untreated

NOEL: 50 mg/kg/day as supplied (20 mg/kg/day as SDMC)

LOEL: 150 mg/kg/day as supplied (60 mg/kg/day as SDMC)

Results: Dermal irritation was observed at dosing site in mid- and high-dose group animals. There was no histologic evidence of systemic toxicity in any group of animals. White blood cell and platelet count were reduced at the high dose level. Additional study information is confidential and compensable under FIFRA.

Method: FIFRA 82-3
 GLP: Yes
 Test substance: Aquatreat SDM sodium dimethyldithiocarbamate 40% aqueous solution
 Reference: Alco Chemical Division, National Starch and Chemical Company; Exxon Biomedical Sciences Incorporated, 1986
 Reliability: (1) Valid without restrictions

***5.5 GENETIC TOXICITY IN VITRO**

A. BACTERIAL TEST

Type: Ames
 System of testing: *Salmonella typhimurium*, strains TA98, TA100, TA 1535, TA 1537, TA 1538
 Concentration: Without Activation: 3333 mg/plate
 With Activation: 3333 mg/plate
 Metabolic activation: With and without
 Results:
 Cytotoxicity conc: With metabolic activation: 6667 mg/plate
 Without metabolic activation: 667 mg/plate
 Precipitation conc: > 6667 mg/plate
 Genotoxic effects:
 With metabolic activation: positive in strains TA100, TA 1535 and TA 1537
 Without metabolic activation: positive in strains TA100, TA 1535 and TA 1537
 Method: OPPTS 870.5100
 GLP: Yes
 Test substance: Aquatreat SDM (40% SDDC in water)
 Remarks: Additional study information is confidential and compensable under FIFRA.
 Reference: Alco Chemical Division, National Starch and Chemical Company; Microbiological Associates, Inc., 1986
 Reliability: (1) Acceptable without restrictions

B. NON-BACTERIAL IN VITRO TEST

Type: Unscheduled DNA Synthesis Assay
 Species/strain: Rats, Sprague-Dawley
 Concentration: 0, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0 and 6.0 µg/ml
 Control group: Yes; Positive Control (2-AAF), negative control and solvent control (EtOH)
 Results:
 Cytotoxicity conc: 2.0 µg/ml
 Precipitation conc: > 6.0 µg/ml
 Genotoxic effects: None at any dose tested.
 Method: OPPTS 870.5550
 GLP: Yes
 Test substance: Aquatreat SDM (40% SDMC)

Remarks: The test substance was considered to be not active in the Rat UDS Assay. Additional study information is confidential and compensable under FIFRA.

Reference: Alco Chemical Division, National Starch and Chemical Company; SITEK Research Laboratories, 1993

Reliability: (1) Valid without restriction

***5.6 GENETIC TOXICITY IN VIVO**

5.7 CARCINOGENICITY

Species/strain: Rats, Fischer 344

Sex: Male/Female

Route of Administration: dietary admixture

Exposure period: 104 weeks starting when rats were six weeks old

Frequency of treatment: Daily, seven days/week

Number of animals: 50 per sex per group

Post exposure observation period: No data

Dose: 0, 1250, 2500 ppm in diet
(approximately 0, 62.5 or 125 mg/kg bw)

Control group: Sixteen untreated males, 20 untreated females

NOEL: Not Determined

LOEL: Not Determined

Results: Groups of 50 rats of each sex were administered sodium diethyldithiocarbamate at one of two doses, either 1,250 or 2,500 ppm, for 104 weeks. Matched controls consisted of 16 untreated male rats and 20 untreated female rats. All surviving rats were killed at the end of administration of the test chemical.

Mean body weights of all dosed groups of rats and mice were lower than those of corresponding controls and were dose related throughout the bioassay except those of the low-dose male rats, which were essentially unaffected by administration of the test chemical. Survival of the rats was unaffected, and no other clinical signs could be related to administration of the test chemical; thus, the animals may have been able to tolerate higher doses. Sufficient numbers of dosed and control animals of each sex were at risk for the development of late-appearing tumors.

No tumors occurred in the rats or mice of either sex at incidences that were significantly higher in the dosed groups than in the control groups. It is concluded that under the conditions of this bioassay, sodium diethyldithiocarbamate was not carcinogenic for F344 rats of either sex.

Method: National Cancer Institute Protocol

GLP: Not specified

Test substance: Sodium diethyldithiocarbamate (CAS 148-18-5)

Reference: National Cancer Institute Carcinogenicity Technical Report Serial number 172, 1979. The complete study report is

available at <http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr172.html>.

Reliability: (2) Valid with restrictions; only two dose levels used, GLP status unknown.

Species/strain: Mouse, B6C3F1
Sex: Male/Female
Route of Administration: Dietary admixture
Exposure period: 108 - 109 weeks starting when mice were six weeks old
Frequency of treatment: Daily, seven days/week
Number of animals: 50 per sex per group
Post exposure observation period: No data
Dose: 0, 500, 4000 ppm in diet
Control group: Twenty (20) untreated mice of each sex
NOEL: Not Determined
LOEL: Not Determined
Results: Groups of 50 mice of each sex were administered sodium diethyldithiocarbamate at one of two doses, either 500 or 4,000 ppm, for 108 or 109 weeks. Matched controls consisted of 20 untreated mice of each sex. All surviving mice were killed at the end of administration of the test chemical.
Mean body weights of all dosed groups of mice were lower than those of corresponding controls and were dose related throughout the bioassay. Survival of the mice was unaffected, and no other clinical signs could be related to administration of the test chemical; thus, the animals may have been able to tolerate higher doses. Sufficient numbers of dosed and control animals of each species and sex were at risk for the development of late-appearing tumors.
No tumors occurred in mice of either sex at incidences that were significantly higher in the dosed groups than in the control groups. It is concluded that under the conditions of this bioassay, sodium diethyldithiocarbamate was not carcinogenic for B6C3F₁ mice of either sex.

Method: National Cancer Institute Protocol

GLP: Not specified

Test substance: Sodium diethyldithiocarbamate (CAS 148-18-5)

Reference: National Cancer Institute Carcinogenicity Technical Report Serial number 172, 1979. The complete study report is available at <http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr172.html>.

Reliability: (2) Valid with restrictions; only two dose levels used, GLP status unknown.

Species/strain: Mouse, C57BL/6 and C3H/Anf
Sex: Male/Female
Route of Administration: Oral intubation for three weeks, then dietary admixture for 17 months
Exposure period: Eighteen months starting when mice were seven days old

Frequency of treatment: Daily, seven days/week
Number of animals: Eighteen per sex per strain
Post exposure observation period: No data
Dose: 560 ppm in diet (approximately 215 mg/kg)
Control group: positive and negative (vehicle only)
NOEL: Not Determined
LOEL: Not Determined
Results: The maximum tolerated dose for testing was determined by a sequence of studies during which the maximal levels resulting in no mortality was determined for a single dose, for six daily doses, and then for nineteen daily doses. Seven day old mice were fed the test article in distilled water vehicle until they were 28 days old. After weaning at 4 weeks, the test compound was mixed directly into their food. Animals were sacrificed after 18 months on test. The postmortem procedure included an external examination and a thorough examination of thoracic and abdominal cavities, with histologic examination of major organs and of all visible lesions. The cranium was not dissected. The entire carcass and all internal organs were fixed and saved. Blood smears were made on all mice before sacrifice, and then examined in cases showing splenomegaly or lymphadenopathy. Statistical analysis included the chi-square test for heterogeneity of proportions after adjustment of stratification (Armitage, 1966), ordinary chi-square tests, regression analyses, the Mantel-Haenszel procedure, and the weighted geometric mean. Seven different chemicals were used as positive controls and were administered via intubation: Ethylcarbamate (158 mg/kg), Ethyleneimine (4.64 mg/kg), Amitrol (1000 mg/kg), Aramite (464 mg/kg), Dihydrosafrole (464 mg/kg), Isosafrole (215 mg/kg) and Safrole (464 mg/kg).

The results of this study were classified "equivocal." Oral administration of the test compound at the maximum tolerated dose resulted in an elevation of tumor incidence in an uncertain range. The positive control chemicals produced the expected incidence and types of tumors in the test animals. The study authors suggest that either additional statistical evaluation and/or experimentation